Defined and Scalable Differentiation of Human Oligodendrocyte Precursors from Pluripotent Stem Cells in a 3D Culture System.

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Public Summary:
Oligodendrocyte precursor cells (OPCs) offer considerable potential for the treatment of demyelinating diseases and injuries of the CNS, including spinal cord injury, side effects of cancer radiation therapy, and inherited conditions. However, generating large quantities of high-quality OPCs remains a substantial challenge that impedes their therapeutic application. Here, we show that OPCs can be generated from human pluripotent stem cells (hPSCs) in a three-dimensional (3D), scalable, and fully defined thermoresponsive biomaterial system. We used CRISPR/Cas9 to create a NKX2.2-EGFP human embryonic stem cell reporter line that enabled fine-tuning of early OPC specification and identification of conditions that markedly increased the number of OLIG2+ and NKX2.2+ cells generated from hPSCs. Transplantation of 50-day-old OPCs into the brains of NOD/SCID mice revealed that progenitors generated in 3D without cell selection or purification subsequently engrafted, migrated, and matured into myelinating oligodendrocytes in vivo. These results demonstrate the potential of harnessing lineage reporter lines to develop 3D platforms for rapid and large-scale production of OPCs.

Scientific Abstract:
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